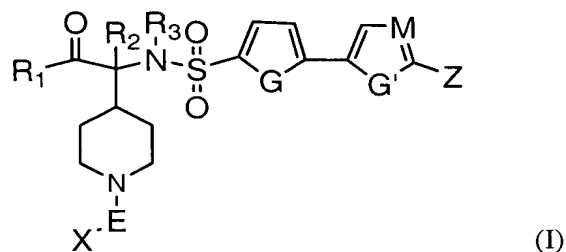


What is claimed is:

1. A compound having a structure according to Formula (I):



wherein:

- (A)  $R^1$  is -NHOH;
- (B)  $R^2$  is selected from hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl and heteroarylalkyl;
- (C)  $R^3$  is selected from alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocycloalkyl, arylalkyl and heteroarylalkyl;
- (D) E is selected from a covalent bond,  $C_1$ - $C_4$  alkyl,  $-C(=O)-$ ,  $-C(=O)O-$ ,  $-C(=O)N(R^4)-$ ,  $-SO_2-$ , or  $-C(=S)N(R^4)-$ , where  $R^4$  is selected from hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl and heteroarylalkyl; or  $R^4$  and X join to form a ring as described in (E)(2);
- (E) (1) X is selected from hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl and heterocycloalkyl; or  
(2) X and  $R^4$  join to form a substituted or unsubstituted, monocyclic heterocycloalkyl having from 3 to 8 ring atoms of which 1 to 3 are heteroatoms;
- (F) G is selected from  $-S-$ ,  $-O-$ ,  $-N(R^5)-$ ,  $-C(R^5)=C(R^{5'})-$ ,  $-N=C(R^5)-$ , and  $-N=N-$ , where  $R^5$  and  $R^{5'}$  each is independently selected from hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, cycloalkyl and heterocycloalkyl;
- (G)  $G'$  is selected from  $-S-$ ,  $-O-$ ,  $-N(R^6)-$ ,  $-C(R^6)=C(R^{6'})-$ ,  $-N=C(R^6)-$ , and  $-N=N-$ , where  $R^{6'}$  and  $R^6$  each is independently selected from hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, cycloalkyl and heterocycloalkyl;

(H) M is selected from -CH- and -N-; and

(I) Z is  $-(CR^7R^7')_a-L-R^8$ , where:

- (1)  $a$  is from 0 to about 4;
- (2) each  $R^7$  and  $R^7'$  is independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, halogen, haloalkyl, hydroxy and alkoxy;
- (3) L is selected from a covalent bond, -O-,  $-SO_b-$ ,  $-C(=O)-$ ,  $-C(=O)N(R^9)-$ ,  $-N(R^9)-$  and  $-N(R^9)C(=O)-$ ; where  $b$  is from 0 to 2 and  $R^9$  is selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalkyl, heteroaryl, cycloalkyl, heterocycloalkyl and haloalkyl; or  $R^7$  and  $R^9$ , together with the atoms to which they are bonded, join to form an optionally substituted heterocyclic ring containing from 5 to 8 atoms of which 1 to 3 are heteroatoms; and
- (4)  $R^8$  is selected from hydrogen, alkyl, alkenyl, alkynyl, halogen, heteroalkyl, haloalkyl, aryl, heteroaryl, cycloalkyl and heterocycloalkyl; or  $R^8$  and  $R^9$ , together with the atoms to which they are bonded, join to form an optionally substituted heterocyclic ring containing from 5 to 8 atoms of which 1 to 3 are heteroatoms;

or an optical isomer, diastereomer or enantiomer for Formula (I), or a pharmaceutically-acceptable salt, or biohydrolyzable amide, ester, or imide thereof.

2. The compound of Claim 1 wherein  $R^2$  is hydrogen or alkyl.
3. The compound of Claim 1 wherein E is selected from a bond,  $C_1$ - $C_4$  alkyl,  $-C(=O)-$ ,  $-C(=O)O-$ ,  $-C(=O)N(R^4)-$  and  $-SO_2-$ .
4. The compound of Claim 3 wherein E is selected from  $C_1$ - $C_2$  alkyl,  $-C(=O)-$ ,  $-C(=O)O-$  and  $-C(=O)N(R^4)-$ .
5. The compound of Claim 3 wherein E is  $-CH_2-$ .
6. The compound of Claim 1 wherein X is selected from hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl and heterocycloalkyl.

7. The compound of Claim 1 wherein X and R<sup>4</sup> join to form a substituted or unsubstituted, monocyclic heterocycloalkyl having from 3 to 8 ring atoms and 1 to 3 ring heteroatoms.
8. The compound of Claim 1 wherein R<sup>3</sup> is selected from alkyl, heteroalkyl, heterocycloalkylalkyl, arylalkyl and heteroarylalkyl.
9. The compound of Claim 1 wherein G is -C(R<sup>5</sup>)=C(R<sup>5'</sup>)-, where R<sup>5</sup> and R<sup>5'</sup> each is hydrogen.
10. The compound of Claim 1 wherein *a* is 0 and L is selected from -O- and -S-.
11. The compound of Claim 10 wherein R<sup>8</sup> is selected from halogen, lower alkyl, lower heteroalkyl and aryl.
12. A compound according to Claim 1 selected from the group consisting of:  
N-Hydroxy-2-[(4'-methoxy-biphenyl-4-sulfonyl)-methyl-amino]-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-acetamide;  
2-[Benzyl-(4'-methoxy-biphenyl-4-sulfonyl)-amino]-N-hydroxy-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-acetamide;  
2-[Ethyl-(4'-methoxy-biphenyl-4-sulfonyl)-amino]-N-hydroxy-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-acetamide;  
2-[(4'-Fluoro-biphenyl-4-sulfonyl)-methyl-amino]-N-hydroxy-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-acetamide;  
N-Hydroxy-2-[(4'-methoxy-biphenyl-4-sulfonyl)-methyl-amino]-2-(1-phenylmethanesulfonyl-piperidin-4-yl)-acetamide; and  
N-Hydroxy-2-[(4'-methoxy-biphenyl-4-sulfonyl)-methyl-amino]-2-(1-phenethyl-piperidin-4-yl)-acetamide.
13. A pharmaceutical composition comprising:
  - (a) a safe and effective amount of a compound of Claim 1; and
  - (b) a pharmaceutically-acceptable carrier.

14. A pharmaceutical composition comprising:
  - (a) a safe and effective amount of a compound of Claim 12; and
  - (b) a pharmaceutically-acceptable carrier.
15. A method for treating a disease associated with unwanted metalloprotease activity in a mammalian subject, the method comprising administering to said subject a safe and effective amount of a compound of Claim 1.
16. A method for treating a disease associated with unwanted metalloprotease activity in a mammalian subject, the method comprising administering to said subject a safe and effective amount of a compound of Claim 12.
17. A method for treating a disorder modulated by metalloproteases, wherein the disorder is chosen from the group consisting of arthritis, cardiovascular disorders, skin disorders, ocular disorders, inflammation and gum disease, the method comprising administering to a mammal in need of such treatment a safe and effective amount of a metalloprotease inhibitor according to Claim 1.
18. The method for treating a disorder according to Claim 17, wherein the disorder is arthritis, and is chosen from the group consisting of osteoarthritis and rheumatoid arthritis.
19. The method for treating a disorder according to Claim 17, wherein the disease is cancer, and the treatment prevents or arrests tumor growth and metastasis.
20. The method for the treating a disorder according to Claim 17, wherein the disorder is a cardiovascular disorder chosen from the group consisting of dilated cardiomyopathy, congestive heart failure, atherosclerosis, plaque rupture, reperfusion injury, ischemia, chronic obstructive pulmonary disease, angioplasty restenosis, and aortic aneurysm.
21. The method for the treating a disorder according to Claim 17, wherein the disorder is an ocular disorder, and is chosen from the group consisting of corneal ulceration, lack of corneal healing, macular degeneration, retinopathy, and pterygium.

22. The method for treating a disorder according to Claim 17, wherein the disorder is gum disease, and is chosen from the group consisting of periodontal disease and gingivitis.
23. The method for treating a disorder according to Claim 17, wherein the disorder is a skin a disorder chosen from the group consisting of wrinkle repair and prevention, U.V. skin damage, epidermolysis bullosa, psoriasis, sclerodema, atopic dermatitis, and scarring.
24. A method for treating inflammatory conditions according to claim 17, wherein said inflammatory condition is chosen from the group consisting of inflammatory bowel disease, Crohn's Disease, ulcerative colitis, pancreatitis, diverticulitis, acne inflammation, bronchitis, arthritis, asthma.
25. A method of preventing or treating a myocardial infarction/progressive ventricular dilation comprising administering to a mammal in need of such treatment, a safe and effective amount of a compound of having a structure according to Claim 1.